

1 CLAIMS

2 What is claimed is:

3 1. A method of determining the likelihood of the presence of a biomolecule
4 comprising the steps of:

5 providing at least one mass signal, wherein said mass signal has a mass
6 signal intensity;

7 comparing said mass signal to a list of known biomolecule fragment
8 signals to determine a potential source biomolecule of said mass signal, wherein said
9 mass signal corresponds to at least one biomolecule fragment of said potential source
10 biomolecule;

11 determining a biomolecule fragment score for said mass signal, wherein
12 said biomolecule fragment score comprises a function of a detection likelihood for said
13 mass signal which defines a biomolecule fragment detection parameter;

14 repeating the steps of comparing and determining a biomolecule fragment
15 score as necessary for additional mass signals;

16 combining said biomolecule fragment scores of said mass signals that
17 correspond to a known biomolecule fragment list for said potential source biomolecule,
18 said combination defining a biomolecule score for said potential source biomolecule;

19 repeating the step of combining as necessary for additional potential
20 source biomolecules; and

21 determining the likelihood of the presence or absence of said biomolecule
22 based on said biomolecule score of said potential source biomolecule that corresponds to
23 said biomolecule.

1 2. The method of claim 1 wherein the step of determining the likelihood of
2 the presence or absence of said biomolecule further comprises the steps of:

3 selecting one of said at least one mass signal, which defines a selected
4 mass signal;

5 comparing said biomolecule scores of at least two potential source
6 biomolecules that correspond to said selected mass signal to determine said potential

7 source biomolecule with a highest biomolecule score;
8 determining that said biomolecule is likely absent if said biomolecule
9 score of the corresponding potential source biomolecule is lower than said highest
10 biomolecule score; and
11 repeating the steps of selecting, comparing biomolecule scores and
12 determining as necessary for additional selected mass signals.

1 3. The method of claim 1 further comprising the step of correcting said mass
2 signal intensity for an isotopic variant of a biomolecule fragment which corresponds to
3 said mass signal.

1 4. The method of claim 1 further comprising the step of calibrating a mass
2 which corresponds to said mass signal.

1 5. The method of claim 1 further comprising the step of removing noise from
2 said mass signal intensity.

1 6. The method of claim 1 further comprising the step of removing artificial
2 background intensity from said mass signal intensity.

1 7. The method of claim 1 wherein said biomolecule fragment detection
2 parameter is proportional to the detection efficiency of said biomolecule fragment that
3 corresponds to said mass signal and a probability that said potential source biomolecule
4 yields said biomolecule fragment as a result of a fragmentation process applied to said
5 potential source biomolecule.

1 8. The method of claim 1 wherein the step of determining a biomolecule
2 fragment score for said mass signal comprises the steps of:
3 determining a detection likelihood for said mass signal which defines said
4 biomolecule fragment detection parameter;
5 determining a mass error for said mass signal from the relative difference
6 between a mass which corresponds to said mass signal and a mass of a known
7 biomolecule fragment which corresponds to said mass signal; and

8 determining said biomolecule fragment score from said mass signal
9 intensity, said biomolecule fragment detection parameter, and said mass error for said
10 mass signal.

1 9. The method of claim 8 wherein said biomolecule fragment score is
2 proportional to said biomolecule fragment detection parameter and said mass signal
3 intensity, and inversely proportional to said mass error for said mass signal.

1 10. The method of claim 1 wherein the step of combining said biomolecule
2 fragment scores comprises excluding a selected biomolecule fragment score from said
3 combination.

1 11. The method of claim 1 wherein the step of combining said biomolecule
2 fragment scores further comprises the steps of:
3 determining a biomolecule fragment count of said potential source
4 biomolecule by counting the number of said mass signals that correspond to said potential
5 source biomolecule;
6 comparing said biomolecule fragment count to the number of said
7 biomolecule fragments on a known biomolecule fragment list for said potential source
8 biomolecule to determine a relative biomolecule match count for said potential source
9 biomolecule;
10 calculating a weighted biomolecule score for said potential source
11 biomolecule from said biomolecule score and said relative biomolecule match count; and
12 determining the likelihood of the presence or absence of said biomolecule
13 based on said weighted biomolecule score.

1 12. The method of claim 1 wherein the step of determining the likelihood of
2 the presence or absence of said biomolecule further comprises the steps of:
3 determining a biomolecule fragment count of said potential source
4 biomolecule by counting the number of said mass signals that correspond to said potential
5 source biomolecule; and
6 determining that said biomolecule is likely absent if said biomolecule

7 fragment count of the corresponding potential source biomolecule is lower than a
8 minimum number.

1 13. The method of claim 1 wherein the step of determining the likelihood of
2 the presence or absence of said biomolecule further comprises the steps of:
3 determining a mass error for said mass signal from the relative difference
4 between a mass which corresponds to said mass signal and a mass of a known
5 biomolecule fragment which corresponds to said mass signal;
6 repeating the step of determining a mass error as necessary for additional
7 mass signals that correspond to a known biomolecule fragment list for said potential
8 source biomolecule;
9 selecting a mass tolerance value; and
10 determining that said biomolecule is likely absent if more than an
11 insignificant number of said mass signals that correspond to said biomolecule have a said
12 mass error that is greater than said selected mass tolerance value.

1 14. The method of claim 1 wherein the step of determining the likelihood of
2 the presence or absence of said biomolecule further comprises the steps of:
3 identifying from about 100 to about 200 of the most intense mass signal
4 intensities to determine the intense mass signals;
5 determining an intense biomolecule fragment count of said potential
6 source biomolecule by counting the number of said intense mass signals that correspond
7 to said potential source biomolecule; and
8 determining that said biomolecule is likely absent if said intense
9 biomolecule fragment count of the corresponding potential source biomolecule is lower
10 than a minimum number.

1 15. The method of claim 14 wherein the step of identifying comprises:
2 determining a mass error for said mass signal from the relative difference
3 between a mass which corresponds to said mass signal and a mass of a known
4 biomolecule fragment which corresponds to said mass signal;
5 selecting a mass tolerance value; and

6 identifying from about 100 to about 200 of the most intense mass signals
7 with a said mass error less than said mass tolerance value and a biomolecule fragment
8 score greater than a minimum number to determine the intense mass signals.

1 16. The method of claim 1 further comprising the step of determining a
2 relative concentration of said biomolecule based on said biomolecule score.

1 17. The method of claim 1, further comprising the steps of:
2 combining at least two of said mass signal intensities to determine a signal
3 intensity score;
4 combining said mass signal intensities of said mass signals which
5 correspond to said known biomolecule fragment list for said potential source biomolecule
6 to determine a potential source biomolecule intensity score;
7 comparing said signal intensity score to said potential source biomolecule
8 intensity score to determine a relative biomolecule intensity corresponding to said
9 potential source biomolecule; and
10 determining the likelihood of the presence or absence of said biomolecule
11 based on said relative biomolecule intensity.

1 18. The method of claim 1, further comprising the steps of:
2 combining at least two of said biomolecule fragment scores to determine a
3 signal biomolecule fragment score;
4 comparing said signal biomolecule fragment score to a said potential
5 source biomolecule score to determine a relative biomolecule detection parameter
6 corresponding to said potential source biomolecule; and
7 determining the likelihood of the presence or absence of said biomolecule
8 based on said relative biomolecule detection parameter.

1 19. The method of claim 1, further comprising the steps of:
2 determining a mass error for said mass signal from the relative difference
3 between a mass which corresponds to said mass signal and a mass of a known
4 biomolecule fragment which corresponds to said mass signal;

repeating the step of determining a mass error as necessary for additional mass signals that correspond to a known biomolecule fragment list for said potential source biomolecule;

combining said mass errors for said mass signals corresponding to said potential source biomolecule to determine a biomolecule mass error for said potential source biomolecule;

repeating the steps determining a mass error and combining said mass errors as necessary for additional potential source biomolecules; and

determining the likelihood of the presence or absence of said biomolecule based on said biomolecule mass error.

20. The method of claim 19 wherein the step of combining said mass errors further comprises weighting a said mass error by the corresponding mass signal intensity to determine a weighted mass error and combining said weighted mass errors to determine said combined biomolecule mass error.

21. The method of claim 1 wherein said step of determining the likelihood of the presence or absence of said biomolecule comprises determining the likelihood of the presence or absence of a protein.

22. The method of claim 1 wherein said step of comparing said mass signals to a list of known biomolecule fragments signals comprises comparing said mass signals to a list of known peptides.

23. A method of determining the likelihood of the presence of a biomolecule comprising the steps of:

providing at least one mass signal, wherein said mass signal has a mass signal intensity;

comparing said mass signal to a list of known biomolecule fragment signals to determine a potential source biomolecule of said mass signal, wherein said mass signal corresponds to at least one biomolecule fragment of said potential source biomolecule;

9 determining a biomolecule fragment score for said mass signal, wherein
10 said biomolecule fragment score comprises a function of a detection likelihood for said
11 mass signal which defines a biomolecule fragment detection parameter;
12 repeating the steps of comparing and determining a biomolecule fragment
13 score as necessary for additional mass signals;
14 combining said biomolecule fragment scores of said mass signals that
15 correspond to a known biomolecule fragment list for said potential source biomolecule,
16 said combination defining a biomolecule score for said potential source biomolecule;
17 repeating the step of combining as necessary for additional potential
18 source biomolecules; and
19 determining whether said biomolecule should be subjected to MS-MS
20 analysis based on said biomolecule score of said potential source biomolecule that
21 corresponds to said biomolecule.

1 24. The method of claim 23 wherein said biomolecule fragment detection
2 parameter is proportional to the detection efficiency of said biomolecule fragment that
3 corresponds to said mass signal and a probability that said potential source biomolecule
4 yields said biomolecule fragment as a result of a fragmentation process applied to said
5 potential source biomolecule.

1 25. The method of claim 23 wherein the step of determining a biomolecule
2 fragment score for said mass signal comprises the steps of:

3 determining a detection likelihood for said mass signal which defines said
4 biomolecule fragment detection parameter;

5 determining a mass error for said mass signal from the relative difference
6 between a mass which corresponds to said mass signal and a mass of a known
7 biomolecule fragment which corresponds to said mass signal; and

8 determining said biomolecule fragment score from said mass signal
9 intensity, said biomolecule fragment detection parameter, and said mass error for said
10 mass signal.

1 26. The method of claim 25 wherein said biomolecule fragment score is
2 proportional to said biomolecule fragment detection parameter and said mass signal
3 intensity, and inversely proportional to said mass error for said mass signal.

1 27. The method of claim 23 wherein the step of combining said biomolecule
2 fragment scores comprises excluding a selected biomolecule fragment score from said
3 combination.

1 28. An article of manufacture having computer-readable program means for
2 performing the method of claim 1 embodied thereon.

1 29. An article of manufacture having computer-readable program means for
2 performing the method of claim 23 embodied thereon.

1 30. An apparatus for determining the likelihood of the presence of a
2 biomolecule based on biomolecule fragment detection likelihood, the apparatus
3 comprising:
4 a biomolecule fragment separation apparatus providing at least one mass
5 signal, wherein said mass signal has a mass signal intensity;
6 a first memory element storing said mass signal provided by said
7 biomolecule fragment separation apparatus;
8 a second memory element storing a list of known biomolecule fragment
9 signals;
10 a third memory element storing a comparator accessing said first memory
11 element and said second memory element to determine if a mass signal stored in said first
12 memory element matches a biomolecule fragment signal in said second memory element;
13 a fourth memory element storing a mass signal-biomolecule fragment
14 signal match determined by said comparator;
15 a fifth memory element containing a weight generator accessing said first
16 memory element and said fourth memory element for determining a biomolecule
17 fragment score for said mass signal;
18 a sixth memory element storing the biomolecule fragment scores;

19 a seventh memory element containing a combination generator accessing
20 said third memory element and said sixth memory element for combining said
21 biomolecule fragment scores of said mass signals that correspond to a known
22 biomolecule fragment list for a potential source biomolecule, said combination defining a
23 biomolecule score for said potential source biomolecule; and
24 an output device providing an output display of at least one of said
25 biomolecule scores.

1 31. The apparatus of claim 30 wherein said biomolecule fragment separation
2 apparatus comprises a MALDI ionization instrument.

1 32. The apparatus of claim 30 wherein said biomolecule fragment separation
2 apparatus comprises a time-of-flight mass spectrometer.

1 33. The apparatus of claim 30 wherein said output device comprises a
2 computer.